REMARKS

The Office Action has maintained the Restriction Requirement and has withdrawn from consideration Claim 55.

The Office Action has rejected Claims 47-54 under 35 U.S.C. §112, first paragraph, in two separate rejections, for allegedly failing to describe the claimed subject matter in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time that the application was filed. In addition, Claims 47-55 have been rejected under 35 U.S.C. §112, first paragraph, for allegedly being non-enabling. Claims 37, 53 and 54 are rejected under 35 U.S.C. §112, second paragraph, for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Further, Claims 47-51 are rejected under 35 U.S.C. §102(b) as defining subject matter which is allegedly anticipated by the teachings in WO/96140148 for which Malfroy-Camine are inventors. ("Mulfroy-Camine"). Finally, claims 47-54 are rejected under 35 U.S.C. §103(a) as defining subject matter which is allegedly rendered obvious by the teachings of Malfroy-Camine in view of the teachings of U.S. Patent No. 5,004,697 to Pardridge ("Pardridge")

Applicants have amended the claims, which when considered with the comments herein, are deemed to place the present case in condition for allowance. Favorable action is respectfully requested.

At the outset, before discussing the Office Action on the merits, applicants wish to thank Examiner Kosar for the kindness and courtesy extended to applicants' representative during the telephone interview on July 28, 2008. During the telephone interview, applicants' representative and Examiner Kosar discussed a proposed claim, which is now Claim 56.

Examiner Kosar indicated that he was favorably disposed towards the proposed claim. In addition, applicants further discussed adding a claim to treat Alzheimer's disease, using claim language like that recited in Claim 56; again Examiner Kosar indicated that he was favorably disposed to this added claim, but Examiner Kosar also indicated that the claim should define the patient population

In accordance with the discussions with Examiner Kosar, applicants have rewritten the claims. Support for the rewritten subject matter is found throughout the specification. For example, support for Claim 56 is found on Page 4, Line 5 to Page 8, Lines 3-7 and Page 11, Line 1 to Page 12, Line 18 of the instant specification. Support for Claim 57 is found on Page 12, Lines 1-18 of the instant specification. Claims 58-65 are old claims 48-55. Claims 66 and 67 are supported by the disclosure on Page 8, Line 33 to Page 9, Line 10 and Page 10, Line 18 to Page 14, Line 3 of the instant specification. Claims 67-70 recite the subject matter in claims 52-55.

No new matter is added to the specification.

Pursuant to the first rejection of Claims 47-54 under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with written description requirement under 35 U.S.C. §112, first paragraph, the Office Action alleges that there is no written support for the language, "solubilizing Aβ deposits in the Alzheimer's patient". Although applicants disagree; however, to advance prosecution, applicants cancelled Claims 47-54 and added new Claims 56-70. As discussed hereinabove, these new claims are supported by the instant specification. Moreover, the claims do not recite the alleged offending language. Thus, the first rejection under 35 U.S.C. §112, first paragraph is obviated; withdrawal thereof is respectfully requested.

Pursuant to the second rejection of Claims 51-54 under 35 U.S.C. §112, first paragraph, for failing to comply with written description requirement, the Office Action alleges that there is no written descriptive support for the language, "solubilizing β amyloid peptide with a metal complex." Again, applicants reiterate that they disagree. Nevertheless, to advance prosecution, applicants have cancelled Claims 47-54 without prejudice and added new Claims 56-70, which as discussed hereinabove, is supported by the instant specification. The claim language in these added claims does not utilize the language, "solubilizing β-amyloid peptide. Thus, this rejection under 35 U.SC. §112, first paragraph, is obviated; withdrawal thereof is respectfully requested.

Pursuant to the rejection of Claims 47-55 under 35 U.S.C. §112, first paragraph, the Office Action alleges that the claimed subject matter does not provide enablement for solubilization of Aβ in Alzheimer's patient with any metal complex. According to the Office Action, the limitation of the method was not found in the filed disclosure and the Office Action concludes that the claimed subject matter cannot be enabled. The Office Action, however, alleges that application is enabling for inhibiting the binding of specific metal compelxed to β-amyloid peptide.

It is respectfully submitted that the present specification is enabling for one of ordinary skill in the art to make and use the claimed invention, as presented. Although the Office Action alleges that claims drawn to solubilization of Aβ deposits in an Alzheimer's patient with metal complex is non-enabled and although applicants disagree with this assessment, that allegation is moot since the claims have been amended to delete the language, solubilization of Aβ in Alzheimer's patients."

The Office Action acknowledges that the specification enables inhibiting the binding of metal ions to β-amyloid peptide with BRI7161, BRI7159, BRI7158, BRI7080 or BRI7103 or the compounds specifically identified in the specification and prior art. However, the Office Action alleges that the specification does not provide enablement for inhibition of the binding of metal ions to the β-amyloid peptide, or treating Alzheimer's disease with all or any metal complexes. According to the Office Action, the specification has provided compounds asserted to be useful in the methods and provides *in vitro* testing and *ex vivo* (e.g. NMR) testing for several compounds. However, the Office Action alleges that the specification does not provide sufficient guidance, including working or prophetic examples, to show that any compound, other than BRI7161, BRI7159, BRI7158, BRI7080 or BRI7103, would work in treating Alzheimer's disease.

In the first instance, Applicants respectfully submit that the present invention is predicated in part on the elucidation that a metal complex, which prevents binding of metal ions to the beta-amyloid protein by competing with the metal ions for at least one histidine residue of Aβ, can thereby solubilize aggregated beta-amyloid deposits in the brains of individuals with Alzheimer's disease. Applicants respectfully submit that prior to the present invention it had been believed that treatment of Alzheimer's disease required binding of the free metal ions, which would therefore not be available for binding to the Aβ. Thus, Applicants respectfully submit that the present invention provides a unique approach to the treatment of Alzheimer's disease.

Moreover, the pending claims now define the metal complex to be a Mn, Co, Ni, Cu, Zn, Ru, Pd, Ag, Cd, Pt, Au, Rh or Hg complex. As discussed above with respect to the written description rejection, the specification on page 4, lines 20-24, teaches that the compound

binds to at least one histidine residue selected from the group consisting of His6, His13 and His14 of the N-terminal loop of β-amyloid peptide. Applicants submit that the specification on page 8, lines 19-25 and page 11, lines 1-21 further delineates that metal ions capable of binding to the imidazole nitrogen of histidine include Mn, Co, Ni, Cu, Zn, Ru, Pd, Ag, Cd, Pt, Au, Rh and Hg, and complexes of these metals are expected to react with beta-amyloid. The specification on page 14, line 1 to page 15, line 23, and page 22, Table 1 and lines 10-16 describes specific examples of metal complexes for use in conjunction with the methods claimed by the present application.

The Office Action alleges that it does not believe that the compounds of the present invention are useful for treating Alzheimer's disease. It alleges that the state of the art is unpredictable. Further, it cites different references to support its allegations that there is no cure for Alzheimer's disease. However, it does not cite any reference that refutes the teaching in the present specification metal complexes of the present invention are not useful for treating Alzheimer's disease.

Nevertheless, the utility of the present invention for treating Alzheimer's disease is quite credible. The Office Action mentions quite a number of drugs, which are being used to treat Alzheimer's disease. Moreover, the Office Action cites WO 96-28471, which teaches a compound inhibits amyloid aggregation and/or neurotoxicity can be used to treat Alzheimer's disease. Thus, the Office Action is inherently admitting that there is credibility for the metal complexes of the present invention to be useful for treating Alzheimer's disease.

Applicants respectfully submit that the United States Patent and Trademark Office has not met its burden in establishing that the application is non-enabling. In order to make a proper rejection, the Office Action has the initial burden to establish a reasonable basis to

question the enablement for the claimed invention. In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1515 (Fed. Cir. 1993). Case law has held that the specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for an enabling support. In re Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). As stated by the Marzocchi Court, "it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." Id. 439 F.2d at 224, 169 USPQ at 370.

Here, the Office Action has not provided any scientific rationale supporting its allegation that the full scope of the present invention is not enabled. In particular, the Office Action has not cited any reference, which refutes the teaching of the present invention. Moreover, the Office Action has not provided any evidence, which disputes the utility of the present invention. The Office Action just renders a mere conclusion without providing any evidence whatsoever that supports its belief that the metal complexes of the present invention would not be useful. Without such evidence, the Office Action has improperly shifted the burden to the applicants.

Applicants reiterate the above comments with respect to the assertion in the Office Action that it is unbelievable that compounds can cross the blood brain barrier. Again, reference is made to WO 96/28471 which teaches that the conjugation of a peptide or other target

moiety, such as protein, with the amyloid modulators described therein enhance transport across the blood brain barrier. Thus, it is believable that coupling of the metal complex with a targeting moiety can be used to transport across the blood brain barrier.

Applicants reiterate that the Office Action has again unjustifiably shifted its burden to the applicants, and incorporate by reference the above comments with respect to the treatment of Alzheimer's disease.

Accordingly, Applicants respectfully submit that the specification provides sufficient guidance for one skilled in the art to make recited metal complex and use them in the presently claimed method, without undue experimentation, a position, which Examiner Kosar concurs. (See Interview Summary Record). Therefore, in view of the foregoing, Applicants respectfully request withdrawal of the enablement rejection under 35 U.S.C. §112, first paragraph.

Claims 31-37, 40, 41, 44 and 45 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by WO 96/40148 to Malfroy-Camine. The Examiner alleges that Malfroy-Camine teaches a method for preventing, arresting or treating a free radical-associated disease, including Alzheimer's disease, by the administration of certain salen metal complex.

Applicants observe that the salen metal complex disclosed by Malfroy-Camine is characterized by a general formula as shown in the reference, as well as on page 10 of the Official Action. However, as claimed, the metal complexes of the present invention are metal porphyrin complexes, metal phenanthroline complexes, none of which are metal salen complexes. Thus, Malfray-Camine does not anticipate the subject matter of any of the claims; withdrawal of this rejection is respectfully requested.

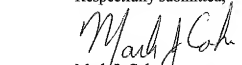
Pursuant to the rejection of Claims 47-54 under 35 U.S.C. §103(a), the Office Action cites Malfray-Camine in view of Pardridge.

Applicants reiterate the comments, hereinabove. Malfray-Camine discloses the use of a salen metal complex for preventing, arresting or treating a free-radial associated, disease state, such as Alzheimer's disease. It does not teach, disclose or suggest the use of a metal complex of a bipyridine, porphyrin or a 1,10-phenanthrolene, as claimed.

Pardridge does not overcome the shortcomings of Malfray-Camine. As described in the Office Action, Pardridge teaches modifying antibodies for delivery through the blood barrier for neuropharmaceuticals. It teaches that the antibody is for the amyloid peptide of Alzheimer's disease. It does not teach, disclose or suggest the use of a metal complex of a bipyridine, porphyrin or a 1,10-phenanthroline, as claimed. Therefore, the combination of Malfray-Camine and Pardridge does not teach, disclose or suggest the use of a metal complex of bipyridine, porphyrin or a 1,10-phenanthrolene, as claimed, a position with which the USPTO concurs (See Interview Summary Record). Therefore, this rejection under 35 U.S.C. §103 is obviated; withdrawal thereof is respectfully requested.

Thus, in view of the Amendment to the Claims and the Remarks hereinabove, it is respectfully submitted that the present case is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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